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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 12/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,633	CHARLES ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *4-11,13-15,19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,12,16-18 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/7/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is the First Office Action on the Merits of the application filed 28 July 2003 as a continuation of application 09/722,342 filed 2 November 2000, which claims benefit of provisional application 60/172,146, filed 17 December 1999. The preliminary amendment filed 20 February 2004 has been entered. Claims 1-21, as originally filed, are pending.

Election/Restrictions

Applicant's election of Group I (claims 1-3, 12, 16-18 and 21) in the reply filed on 15 November 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 4-11, 13-15, 19 and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the 15 November reply.

Claims 1-3, 12, 16-18 and 21 are presently under consideration.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Methods for provision of appetite control agents.

Claim Objections

Claims 1 and 12 are objected to because of the following informalities:

Claim 1 recites "CPR19" rather than "GPR19" in line 3.

Claim 12 is objected to because it depends from non-elected claims. Incorporation of the limitations of the non-elected claims into claim 12 would be remedial.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

Claim 12 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 12, 16-18 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the Invention and Breadth of the Claims:

The claims are directed to a method for the provision of an appetite control agent comprising (i) using one or more agonists or antagonists of a G protein coupled receptor GPR19 as test compounds in one or more appetite control test procedures; and (ii) selecting an active compound for use as an appetite control agent. Therefore, the nature of the invention is directed toward a method of identifying agonists and/or antagonists of GPR19 receptor that are effective in appetite control.

State of the Art, Amount of Direction provided and existence of working examples:

The prior art teaches the nucleotide sequence of the GPR19 from human, rat and mouse. The specification discloses that a number of products are being developed for the treatment of obesity and eating disorders and that these are targeted against a wide range of biological targets (page 1, line 25) that include G-protein coupled receptors. Further, the specification discloses that the Applicants have identified that the mRNA encoding GPR19 is differentially expressed in murine appetite/obesity models and that it follows that non-peptidic compounds acting on

GPR19 will have utility in controlling food intake and metabolic processes (bridging paragraph, pages 1 and 2). However, the specification also teaches that the natural ligand for GPR19 is not yet known (page 3, line 18) and discloses a contemplated method of transfecting mammalian cells with the GPR19 clone and screen to find natural or synthesized ligands that will activate GPR19. The specification further contemplates the use of these transfected cell lines to identify compounds that act as agonists of GPR19 by activating the receptors and those that act as antagonists by by antagonizing the activation effect of a GPR19 ligand (page 3, line 26). Further experiments contemplated by the Applicants include genetically engineering the GPR19 receptor (page 8, lines 3-8) and using it to screen for antagonists of the constitutively active mutant receptor in the absence of a ligand. Further, the specification contemplates what can be done "once the natural ligand of GPR19 becomes known" (page 12, line 8) and that chemical compounds can then be tested for their ability to activate or antagonize the activity of the GPR19 receptors (page 13, line 2-4).

The only correlation provided in the specification between the GPR19 receptor and appetite control and/or obesity is the differential expression of the receptor in murine obesity models. This guidance is not sufficient to establish that agonists and antagonists of the GPR19 receptor would be pharmaceutically effective in appetite control test procedures and in a method of appetite control. Halban et al. (2001; Diabetes, volume 50, pp2181-2191; made of record in the IDS filed 7 November 2005) in their review on the gene and cell-replacement therapy in the treatment of diabetes, caution that "we not forget the age-old adage that a rodent is not a human in more ways than just appearance" (page 2187, left column, paragraph 2, lines 5-7). Halban et al. further state that the use of rodent models may be useful for certain aspects of the metabolism,

it has the potential to be misleading for others, including glucose disposal (page 2187, left column, paragraph 3, lines 1-4). They further state that when using animal models to test new systems, one must keep in mind that the efficacy of glucose uptake by insulin-independent mechanisms in animals is commonly greater than in humans and that simply translating animal findings as the likely observation in humans may be risky (page 2187, left column, paragraph 3, lines 26-31). Thus, the results obtained in murine models cannot predictably be extended to other animal systems including human.

Furthermore, Williams (2003) *Curr. Opin. Pharmacol.* 3:571-577 teaches that identification of gene variation is only the first step in a complex and unpredictable process of validating a gene as a therapeutic target. In particular, Williams teaches, "target validation, especially that related to novel genomically derived targets, is a highly complex and resource-intensive process that has added considerably to the cost of drug discovery [], with currently little to show in terms of either novel validated drug targets or an increase in the number of compounds in development" (paragraph bridging pages 571-572). Thus, Williams teaches that merely identifying a gene as differentially expressed in a disease state does not establish the gene product as a target for pharmaceutical intervention in that disease.

Further, the specification fails to disclose any chemical compounds that might have any effect on the GPR19 receptor in the form of agonists or antagonists. The specification also fails to disclose any correlation between any potential chemical compounds acting as agonists and/or antagonists of the GPR19 receptor and a method of appetite control. Although prior art teaches the use of chemical compounds that are used in appetite control and/or obesity, neither the prior art nor the specification teach whether these compounds can act as agonists and/or antagonists of

the GPR19 receptor. Further, the specification fails to disclose any pharmaceutical activity for these potential chemical compounds that are expected to be identified by the method of the instant invention. In addition, the specification fails to teach the pharmaceutically effective dosages, frequency of administration, such that one of skill can accept the method of the instant invention and practice it without undue experimentation.

In the absence of the availability of a ligand for GPR19, and lack of knowledge on the biological characterization of the said ligand of GPR19 receptor, a skilled artisan would be required to engage in undue experimentation to identify chemical compounds that would act as agonists and/or antagonists that will have an effect on the activity of the GPR19 receptor and to be able to use them in a method of appetite control by providing a pharmaceutically effective amount of one or more chemical compounds to an individual. Although the activity of the GPR19 receptor is known to have an effect on the levels of intracellular signaling molecules such as cyclic AMP, intracellular calcium ions or arachidonic acid metabolite release (specification, page 3, lines 11-13), the lack of knowledge on the natural ligand of the receptor and on which chemical compounds might be effective as agonists or antagonists of a GPR19 receptor leads one of skill to engage in undue experimentation to identify and use the agonists or antagonists of a GPR19 receptor in appetite control test procedures as claimed. The specification does not provide sufficient guidance such that one of skill in the art would accept that their method would result in a therapeutic outcome and be able to practice the method using the guidance provided in the specification.

Predictability of the Art, Amount of Experimentation and Skill level of the artisan:

Although the skill of an artisan in this subject area is considered to be very high, it would require undue experimentation on the part of an artisan to make and use the invention as specified and use the invention as claimed. The specification and the working examples do not provide sufficient guidance to practice the invention as claimed. Therefore, in the absence of specific guidance and working examples, the use of the claimed method is unpredictable. Further, "appetite control" usually refers to suppressing appetite. The specification does not provide a definition for this phrase. In the absence of an explicit definition in the specification, interpreted as broadly as reasonable, the phrase "appetite control", as claimed, includes stimulating appetite as well as suppressing appetite. The specification (page 1, line 4) discloses the interchangeable use of the terms appetite control and obesity and discloses the contemplated use of GPR receptors in treating obesity (page 1, line 25). Thus, the phrase "appetite control" as disclosed in the specification refers exclusively to suppressing appetite. The specification does not contemplate identifying agents that stimulate appetite. If that is the meaning within which the phrase "appetite control" is used in the instant case, it is, then, unpredictable how and why both agonists and antagonists of GPR19 receptor could be used as appetite control agents. Because, agonists and antagonists have opposing effects, they, therefore, cannot both be used to provide the same pharmacological action (i.e., appetite control, as claimed in the instant case). Further, the claims encompass both stimulating as well as suppressing appetite, and the specification deals with only suppression of appetite. In such a situation, one skilled in the art would not know how to use the invention as claimed, without undue experimentation. In view of the limited guidance in the specification, and limited prophetic examples, and the unpredictability of the art,

one skilled in the art would be required to engage in undue experimentation, in order to use the invention.

Thus, due to the art recognized unpredictability of achieving therapeutic and correlative effects via extrapolation of murine model behavior to humans, the lack of guidance provided by the specification, the lack of guidance concerning the treatment of obesity and/or appetite control using the claimed method of the instant invention, it would have required undue experimentation to practice the instant invention and the skilled artisan would not have predicted success in using the claimed methods of providing appetite control agents and a method of appetite control using the guidance provided in the specification. Thus the specification does not enable one skilled in the art to use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 12, 16-18 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2 and 12are indefinite in their recitation of "appetite control". The meaning of this phrase is not clear. The specification does not provide a definition for this phrase. In the absence of an explicit definition in the specification, interpreted as broadly as reasonable, the phrase "appetite control", as claimed, includes stimulating appetite as well as suppressing appetite. The specification (page 1, line 4) discloses the interchangeable use of the terms appetite control and obesity and discloses the contemplated use of GPR receptors in treating obesity

Thus, the phrase "appetite control" as disclosed in the specification refers to suppressing appetite. If that is the meaning within which this phrase is used, then it is unclear how both agonists and antagonists, which are agents that usually have opposing effects, can both be used as appetite control agents to suppress appetite. The specification does not contemplate identifying agents that stimulate appetite. Claims 3, 17 and 21 are rejected insofar as they depend from claims 1 or 2.

Claims 1, 2 are indefinite in their recitation of "appetite control test procedures". It is not clear what is encompassed by this phrase. The specification describes ligand binding assays and SPA assays (page 13, line 5) in vitro and in vivo in cell lines to identify the agonists and antagonists and further contemplates using the identified compounds in animal models (page 13, line 22) and discloses a list of parameters that can be measured (page 13, line 31). The specification, however, does not describe any procedures to be used as "appetite test control procedures". Thus it is not clear what this phrase is referring to. Claims 3, 16-18 and 21 are indefinite insofar as they depend from claims 1 or 2.

Claim 12 provides for the use of a transgenic animal, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M Sullivan, Ph.D.
Examiner
Art Unit 1636

DANIEL M. SULLIVAN
PATENT EXAMINER